REMARKS

Reconsideration of this application is respectfully requested in view of the foregoing amendments and the following remarks.

Claims 1-12 and 23-34 are currently pending in this application, with claims 23-34 having been withdrawn from consideration as being drawn to a non-elected invention. By this Amendment, claims 1, 5, and 10 have been amended.

No new matter is presented in this Amendment.

Claim to Priority

The Office Action acknowledged Applicants' claim for foreign priority based on Application No. PCT/GB04/03512, filed on August 16, 2009, and UK Application No. 0319167.3, filed on August 15, 2003. The Office Action required that the priority information be presented in the first sentence of the specification, or in an Application Data Sheet, and indicated that a petition and fee may be required in order for Applicants to rely on the filing dates of these prior applications.

Applicants submit that this reference to the priority information was previously submitted within the time period set forth in 37 C.F.R. § 1.78(a), as it was included with the information transmitted to the U.S. Patent Office by the International Bureau when this national stage entry application was filed. Further, this priority information was correctly shown on the first filing receipt dated April 11, 2007. Applicants therefore respectfully submit that no petition or surcharge is required in order to rely on the filing dates of the prior applications.

Objection to the Specification

The specification was objected to for failing to include the related application data in the first paragraph. The specification has been amended to include this information, and therefore Applicants respectfully request that this objection to the specification be withdrawn.

The specification was also objected to because it contains embedded hyperlinks on pages 14 and 22. In response to this objection, Applicants have amended the specification to delete the embedded hyperlinks. Accordingly, Applicants respectfully request that this objection to the specification be withdrawn.

Notice Regarding Sequence Requirements

The Office Action took the position that the present application fails to comply with the requirements of 37 C.F.R. § 1.821 through 1.825, and referred to a Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures that was allegedly attached to the Office Action.

However, Applicants submit that no Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures was attached to the Office Action. Further, no Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures was found amongst the information contained on the U.S. Patent Office's Private PAIR database relating to this application.

Applicants have amended the specification to insert Sequence ID Nos. for the sequences set forth on pages 3-4. In view of these amendments, Applicants submit that this application is in full compliance with the requirements of 37 C.F.R. § 1.821 through 1.825, and respectfully request that this requirement be withdrawn.

Objections to the Claims

In response to the objections to the claims set forth in the Office Action, Applicants have presented amendments to claims 1, 5, and 10 to present full names at the initial occurrence of acronyms in the claims, and to substitute American English spellings for certain claim terms presented using British English spellings. Accordingly, Applicants respectfully request that the objections to the claims be withdrawn.

Claim Rejections - 35 U.S.C. § 102

Claims 1-4 and 7-8 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Kasturi et al. (*Stroke*, Vol.23, No.9, 1992, pages 1257-1264). Applicants respectfully traverse this rejection.

Kasturi et al. is cited for disclosing that the presence of known RFLPs in the apoprotein A-1-C-III gene cluster were restricted with SacI and PstI and assessed for stroke risk in an American population. *See* abstract.

However, Applicants submit that Kasturi et al. does not concern the diagnosis of stroke, or determination of plasma protein levels.

Kasturi et al. relates to a study conducted to determine genetic risk factors residing in the region of the apolipoprotein A-I, apolipoprotein C-III and apolipoprotein A-IV gene complex. To study this, Kasturi et al. analyzed restriction fragment length polymorphisms (RFLPs) in this region in a group of controls and two groups of patients with carotid artery stenosis (>30% of whom were deemed at risk for stroke). Within these groups, white and black subjects were also studied separately. Kasturi et al. found that there was very little statistically-significant association between RFLPs in the

apolipoprotein genes and those at higher risk of stroke. Table 2 shows that the levels of triglycerides and LDL are significantly higher in the high risk stroke group, while HDL is significantly lower in the same group when compared to controls. However, it should be noted that there is considerable overlap between the ranges. When the plasma lipid levels were studied in the different racial groups, however, these patterns were reversed between the white and black groups (*see* Table 3).

As stated above, Kasturi et al. relates to identifying risk factors for stroke, ***not diagnostic markers of stroke***. The study groups were described as control or high stroke-risk. It was noted that some of the subjects in Group 2 had previously suffered strokes (*see* p. 1258, col. 2), but there was no indication of when those subjects had suffered strokes. Kasturi et al. describes measurement of plasma lipids, but it does not disclose or suggest measurement of levels of any proteins, let alone the levels of apolipoproteins.

Applicants submit that one skilled in the art, having the disclosure of Kasturi et al. before him, would not gain any knowledge of diagnostic protein markers of stroke that are present in a sample of body fluid. Kasturi et al. does not conduct any analysis of patients after stroke, other than including in Group 2 an undefined number of subjects who had suffered strokes at an undisclosed prior time. When reading the Discussion section of Kasturi et al., the skilled artisan would also conclude that the significance of RFLPs in the apolipoprotein gene complex as a risk factor for stroke is low, if present at all, and would not understand that plasma levels of apolipoproteins are modulated during a stroke and may be used as a diagnostic indicator after a stroke. In other words, Kasturi et al. present no evidence nor suggest any association between a subject having a stroke and changes in the levels of apolipoproteins.

Since Kasturi et al. fails to disclose or credibly suggest a link between changes in the concentration of at least one polypeptide selected from Apo C-III, Serum Amyloid A, Apo C-I,

Antithrombin III fragment and Apo A-I in a sample of body fluid, and diagnosis of stroke, Applicants submit that Kasturi et al. does not disclose or suggest the presently-claimed methods.

Accordingly, in view of the amendments and remarks set forth above, Applicants submit that claims 1-4 and 7-8 are not anticipated by Kasturi et al., and respectfully request that the rejection under 35 U.S.C. § 102(b) be withdrawn.

Claim Rejections - 35 U.S.C. § 103

Claims 5 and 12 are rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Kasturi et al. in view of Jackowski et al. (WO 00/52476). The rejection is respectfully traversed.

The disclosure of Kasturi et al. is described above. The Office Action admits that Kasturi et al. fails to disclose the evaluation of multiple polypeptides, and distinguishing between ischemic and hemorrhagic stroke.

Jackowski et al. is cited for disclosing a method for assessing stroke (cerebral injury) via the measurement of multiple markers. The various markers include calbindin-D, myelin basic protein, S-100β, and thrombomodulin. *See* Figure 2. On page 1, Jackowski et al. discloses that stroke is routinely diagnosed with CT scans to assess brain damage. *See* page 1, lines 18-29. The multiple markers may be determined in the same sample or from samples obtained at different time periods. *See* page 12, lines 3-16.

The Office Action takes the position that this allows for patient analysis and monitoring, and that the detection of multiple markers can distinguish and/or differentiate between ischemic and hemorrhagic events. Jackowski et al. allegedly discloses that the determination of a plurality of patient-derived markers is correlated to a subarachnoid hemorrhage.

The Office Action further takes the position that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to evaluate multiple polypeptides, as taught by Jackowski et al., using the methods of Kasturi et al., because Jackowski et al. taught that the detection of multiple markers can distinguish and/or differentiate between ischemic and hemorrhagic events.

However, Applicants submit that nothing in the disclosure of Jackowski et al. remedies the deficiencies of Kasturi et al. set forth above.

Accordingly, in view of the amendments and remarks set forth above, Applicants submit that claims 5 and 12 are not unpatentable over Kasturi et al. and/or Jackowski et al., and respectfully request that this rejection be withdrawn.

Claims 6 and 9-11 are rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Kasturi et al. in view of Yates et al. (U.S. Patent No. 5,538,897). The rejection is respectfully traversed.

The disclosure of Kasturi et al. is described above. The Office Action admits that Kasturi et al. fails to disclose mass spectrometric analysis of the peptide or peptide fragment measurements.

However, Yates et al. is cited for disclosing a method of correlating a peptide fragment with amino acid sequences derived from a database. A peptide is analyzed by a tandem mass spectrometer to yield a peptide fragment mass spectrum (mass fingerprinting). A protein sequence database or a nucleotide sequence database is used to predict/identify the fragment. For each candidate sequence, a plurality (pool) of fragments of the sequences is identified and the masses-m/z ratios of the fragments are predicted and used to form a predicted mass spectrum. See abstract.

The Office Action takes the position that it would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize tandem mass spectrometry database sequence

comparison as taught by Yates et al. to identify the fragments found in the method of Kasturi et al., and that one of ordinary skill in the art would have been motivated to do this because in order to achieve maximal data processing/protein manipulation to determine the parameter of interest.

However, Applicants submit that nothing in the disclosure of Yates et al. remedies the deficiencies of Kasturi et al. set forth above.

Accordingly, in view of the amendments and remarks set forth above, Applicants submit that claims 6 and 9-11 are not unpatentable over Kasturi et al. and/or Yates et al., and respectfully request that this rejection be withdrawn.

CONCLUSION

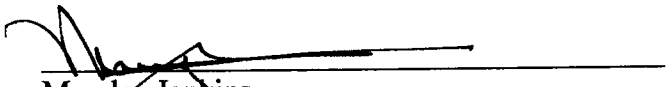
For all of the above reasons, it is respectfully submitted that the claims now pending are in condition for allowance. Accordingly, reconsideration and withdrawal of the outstanding rejections and an issuance of a Notice of Allowance are earnestly solicited.

Should the Examiner determine that any further action is necessary to place this application into better form the Examiner is encouraged to telephone the undersigned representative at the number listed below.

In the event this paper is not considered to be timely filed, the Applicants hereby petition for an appropriate extension of time. The Commissioner is hereby authorized to charge any fee deficiency or credit any overpayment associated with this communication to Deposit Account No. 01-2300, referencing **Atty. Docket No. 108140.00041**.

Date: October 23, 2009

Respectfully submitted,



Marylee Jenkins
Registration No. 37,645
ARENT FOX LLP
1675 Broadway
New York, NY 10019
Tel. No. (212) 484-3945
Fax No. (212) 484-3990
Customer No. 38485